



PATENT APPLICATION

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE APPLICATION OF : ANNAPRAGADA, Ananth, et al.  
TITLE : COMPOSITIONS AND METHODS FOR  
ENHANCING CONTRAST IN IMAGING  
SERIAL NO. : 10/830,190  
FILING DATE : April 21, 2004  
EXAMINER : Not Yet Assigned  
ART UNIT : 1616  
DOCKET NO. : 27428-4

Mail Stop Amendment  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

**DECLARATION UNDER 37 C.F.R § 1.132**

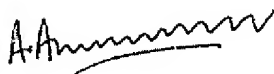
1. Cited against the subject application is the disclosure found in Torchilin et al., Biochim. Biophys. Acta 1996, 1279, 75-83 ("Torchilin").
2. I, Dr. Ananth Annapragada, Ph.D., am an inventor with respect to the subject application. I am an Associate Professor of Bioinformatics, School of Health Information Sciences, The Keck Institute for Computational and Structural Biology & The Graduate School of Biological Sciences, The University of Texas Health Sciences Center at Houston & The Department of Chemical Engineering, The University of Houston.
3. The method of preparation described in Torchilin involves the formation of liposomes from a mixture of PC, cholesterol, PEG-PE, and SA-DTPA. Such liposomes will necessarily exhibit the DTPA molecule on both the outside and

inside of the liposome wall. However, when exposed to the  $\text{In}^{111}$ -citrate complex, only the external DTPA will be bound by the citrate, thus localizing the  $\text{In}^{111}$  on the outside of the liposome exclusively. The reason for this is the  $\text{In}^{111}$ -citrate is a large ionic species, thus bearing a net charge in solution, and possessing very low membrane diffusivity. Penetration of this material into the lipidic bilayer is practically impossible and, thus, the material is excluded from the interior of the liposome. In contrast, amended claims 1 and 25 call for encapsulation of nonradioactive contrast enhancing agent.

4. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under 18 U.S.C. § 1001, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Full name of Declarant: Ananth V. ANNAPRAGADA  
FAMILY NAME IN UPPER CASE

Inventor's signature :



Date : 9-11-07\_\_\_\_\_

Residence/Post : Houston, Texas\_\_\_\_\_

Citizenship : Indian\_\_\_\_\_